

## *REMARKS*

### *The Present Invention and Pending Claims*

Claims 24, 25, 27, 28, 30, 33, and 35-70 are currently pending and directed to a creatine amidinohydrolase (claims 24, 25, 27, 28, 30, 33, 35-37, and 48-54), a method for producing creatine amidinohydrolase (claims 38, 43, 45, 47, 55, and 56), a reagent for determination of creatine in a sample (claims 39, 41, 44, 46, 57-62, and 64-69), and a method for determining creatine in a sample (claims 40, 42, 63, and 70).

### *Amendments to the Claims*

Claim 43-70 are new. Claims 43-47 correspond to claims 38-42, except that claims 43-47 depend from claim 25, rather than claim 24. Claims 48-70 correspond to the original claims 1-23 of the parent application, except that claims 48-70 (a) recite a pI of about 4.5 (rather than about 3.5), (b) specify that the optimum temperature is measured at a pH of about 7.5, and (c) specify that the optimum pH is measured at a temperature of 37° C, as supported by the specification at, e.g, column 7, lines 1-24. Accordingly, no new matter has been added by way of these amendments.

### *The Advisory Action dated May 22, 2003*

The Office did not enter the claim and specification amendments proposed in the "Response to Office Action" dated May 1, 2003. Accordingly, the Office maintained the rejections stated in the Office Action dated November 1, 2002. Specifically, the Examiner rejected claims 24-42 under 35 U.S.C. § 112, first paragraph, as containing subject matter that allegedly was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the patent application was filed, and for alleged lack of enablement. The Office has rejected claims 27, 29, 31, and 33-37 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 24 and 28 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Japanese Patent Application Number 62-099182. Reconsideration of these rejections is hereby requested.

### *Request for Personal Interview*

Applicants respectfully request a personal interview with the Examiner and the Supervisory Primary Examiner to discuss the outstanding issues and this supplemental response to the Office Action. An Applicant Initiated Examiner Interview Request Form is attached hereto, which indicates that the undersigned attorney of record and representatives of the applicant (who will travel from Japan) intend to attend the personal interview.

*Discussion of the Rejection under 35 U.S.C. § 112, first paragraph*

In the Advisory Action dated May 22, 2003, the Office contends that the amendments to the specification, abstract, and claims presented in the "Response to Office Action" dated May 1, 2003, which recite a pI value of 4.5 instead of 3.5, are new matter and will not be entered. Applicants request that the proposed amendments be entered at this time. These amendments do not introduce any new matter for the following reasons.

U.S. Patent 6,080,553 describes three specific novel creatine amidinohydrolases, which can be obtained from the following deposited materials: *Escherchia coli* JM109 (pCRH273M2), *Escherchia coli* JM109 (pCRH273M1), and *Escherchia coli* JM109 (pCRH273M3). By comparison of Tables 2, 4, and 6 set forth in U.S. Patent 6,080,553, it is apparent that the majority of the physicochemical properties are conserved between the novel creatine amidinohydrolases, including the pI value. U.S. Patent 6,080,553 also describes a group of novel creatine amidinohydrolases that include the three specific novel creatine amidinohydrolases disclosed in U.S. Patent 6,080,553.

The accompanying Rule 132 Declaration of Atsushi Sogabe discusses what the disclosure of U.S. Patent 6,080,553 would mean to one of ordinary skill in the art in 1996 (i.e., at the time of the priority date for the present patent application), as well as today.

The ordinary skilled artisan would understand that U.S. Patent 6,080,553 pertains to creatine amidinohydrolases, which are described in various terms, including by reference to isoelectric point, in that patent (Rule 132 Declaration, paragraph 3). The isoelectric point (pI) of a protein can be determined experimentally or from the amino acid sequence of the protein (Rule 132 Declaration, paragraph 4). U.S. Patent 6,080,553 provides the amino acid sequence of wild-type creatine amidinohydrolase derived from *Alcaligenes faecalis* and describes specific mutants thereof (Rule 132 Declaration, paragraphs 5-6). In 1996, one of ordinary skill in the art would have been able to determine the pI values of the wild-type creatine amidinohydrolase and the mutants thereof, as well as any other creatine amidinohydrolases (Rule 132 Declaration, paragraphs 5-6).

One of ordinary skill in the art would have understood in 1996 that U.S. Patent 6,080,553 describes three specific novel creatine amidinohydrolases as well as a group of novel creatine amidinohydrolases that include the three specific novel creatine amidinohydrolases (Rule 132 Declaration, paragraphs 7-8).

If an ordinarily skilled artisan read U.S. Patent 6,080,553 in about 1996, the ordinarily skilled artisan would have recognized that the three specific novel creatine amidinohydrolases described in U.S. Patent 6,080,553 are a representative subset of a group

of novel creatine amidinohydrolases disclosed in U.S. Patent 6,080,553 with a shared set of physicochemical properties (Rule 132 Declaration, paragraph 9). The ordinarily skilled artisan also would have recognized that the pI value would be conserved among the members of this group of novel creatine amidinohydrolases as a function of conserving the function and physiological properties of the novel creatine amidinohydrolases (Rule 132 Declaration, paragraph 9).

If an ordinarily skilled artisan determined that the actual pI value of the three specific novel creatine amidinohydrolases described in U.S. Patent 6,080,553 differed from the pI value reported in U.S. Patent 6,080,553 for those three specific novel creatine amidinohydrolases, the ordinarily skilled artisan would have understood that the actual pI value characterized not only the three *specific* novel creatine amidinohydrolases but also the *group* of novel creatine amidinohydrolases that contained those three specific novel creative amidinohydrolases (Rule 132 Declaration, paragraph 10).

The actual pI value of the three specific novel creatine amidinohydrolases described in U.S. Patent 6,080,553 is about 4.5, rather than the about 3.5 reported in U.S. Patent 6,080,553 (Rule 132 Declaration, paragraphs 11-16). The actual pI values of various other creatine amidinohydrolases also are known to be about 4.5 (Rule 132 Declaration, paragraph 17). Since the pI value of the three *specific* novel creatine amidinohydrolases was determined experimentally to be about 4.5, the pI value of the *group* of novel creatine amidinohydrolases with the three specific novel creatine amidinohydrolases as members also would be understood by one of ordinary skill in the art, reading U.S. Patent 6,080,553, to be about 4.5 (Rule 132 Declaration, paragraph 18).

The amendments presented in the "Response to Office Action" dated May 1, 2003, cannot be considered to introduce new matter, since the specification describes multiple characteristics of the *group* of novel creatine amidinohydrolases, including a deposit of the bacterial strains comprising the three novel creatine amidinohydrolases which are members of the *group* of novel creatine amidinohydrolases recited in the claims, such that upon reading U.S. Patent 6,080,553, together with what was known in the art, at the time of the priority date of the patent application in 1996, one of ordinary skill in the art would have been able to determine that the pI value of the claimed group of novel creatine amidinohydrolases is about 4.5 and would have understood that a pI value of 4.5 was a characteristic of the claimed group of novel creatine amidinohydrolases.

The amendments to the specification, abstract, and claims presented in the "Response to Office Action" dated May 1, 2003, as well as the remarks section of the "Response to Office Action" dated May 1, 2003, are believed to address the remaining concerns of the

Office regarding the Section 112, first paragraph, rejections. Accordingly, Applicants request that the rejections be withdrawn.

*Discussion of the Rejection under 35 U.S.C. § 112, second paragraph*

The Office has rejected claims 27, 29, 31, and 33-37 under Section 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Claims 29, 31, and 34 have been canceled in the "Response to Office Action" dated May 1, 2003. Claims 33 and 35-37 (as well as claims 24 and 25) were presented in the "Response to Office Action" dated May 1, 2003, such that the claims no longer recite pH stability or heat stability. Additionally, claim 27 (as well as claim 25) was presented in the "Response to Office Action" dated May 1, 2003, to recite the temperature at the optimal pH. As such, the indefiniteness rejection is believed to be moot.

*Discussion of the Rejection under 35 U.S.C. § 102(b)*

The Office has rejected claims 24 and 28 under Section 102(b) as allegedly anticipated by Japanese Patent Application Number 62-099182. The pending claims, as presented in the "Response to Office Action" dated May 1, 2003, recite a creatine amidinohydrolase encoded by a nucleic acid sequence obtained by mutation of (a) the nucleic acid sequence of SEQ ID NO:2 or (b) a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:1 with an isoelectric point of about 4.5. JP 62-099182 does not disclose a creatine amidinohydrolase with these characteristics. In that JP 62-099182 does not teach or suggest every element of claim 24 or 28, JP 62 099182 does not anticipate claim 24 or 28, and the Section 102 rejection should be withdrawn.


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*Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

In re Appln. of Sogabe et al.  
Application No. 09/940,941

Respectfully submitted,



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